```
=> d his

     (FILE 'HOME' ENTERED AT 09:09:43 ON 02 JUL 2004)

     INDEX 'ADISCTI, ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, AQUASCI,
     BIOBUSINESS, BIOCOMMERCE, BIOSIS, BIOTECHABS, BIOTECHDS, BIOTECHNO, CABA,
     CANCERLIT, CAPLUS, CEABA-VTB, CEN, CIN, CONFSCI, CROPB, CROPU, DISSABS,
     DDFB, DDFU, DGENE, DRUGB, DRUGMONOG2, ...' ENTERED AT 09:09:59 ON 02 JUL
     2004
               SEA CHINESE HAMSTER OVARY
              ---------
            143    FILE ADISCTI
             58    FILE ADISINSIGHT
              4    FILE ADISNEWS
            181    FILE AGRICOLA
             57    FILE ANABSTR
             29    FILE AQUASCI
            292    FILE BIOBUSINESS
            102    FILE BIOCOMMERCE
          21872    FILE BIOSIS
           4806    FILE BIOTECHABS
           4806    FILE BIOTECHDS
           7592    FILE BIOTECHNO
            621    FILE CABA
           3800    FILE CANCERLIT
          12128    FILE CAPLUS
            294    FILE CEABA-VTB
              2    FILE CEN
             41    FILE CIN
            290    FILE CONFSCI
             38    FILE CROPU
            668    FILE DISSABS
            100    FILE DDFB
           1063    FILE DDFU
            888    FILE DGENE
            100    FILE DRUGB
             12    FILE IMSDRUGNEWS
           1290    FILE DRUGU
             19    FILE IMSRESEARCH
             94    FILE EMBAL
          11079    FILE EMBASE
           5685    FILE ESBIOBASE
             97    FILE FEDRIP
             37    FILE FROSTI
             87    FILE FSTA
            283    FILE GENBANK
             82    FILE HEALSAFE
            515    FILE IFIPAT
            311    FILE JICST-EPLUS
              8    FILE KOSMET
           4885    FILE LIFESCI
          11701    FILE MEDLINE
            676    FILE NIOSHTIC
            221    FILE NTIS
              4    FILE OCEAN
           4352    FILE PASCAL
             14    FILE PHAR
             11    FILE PHARMAML
             68    FILE PHIN
            265    FILE PROMT
             44    FILE PROUSDDR
```

```
     2    FILE RDISCLOSURE
 10523    FILE SCISEARCH
     1    FILE SYNTHLINE
 13373    FILE TOXCENTER
 13597    FILE USPATFULL
   574    FILE USPAT2
     4    FILE VETU
  2276    FILE WPIDS
     4    FILE WPIFV
  2276    FILE WPINDEX
    34    FILE CASREACT
    30    FILE DPCI
  2124    FILE EUROPATFULL
     1    FILE FRANCEPAT
    39    FILE FRFULL
    83    FILE INPADOC
    16    FILE JAPIO
     3    FILE LITALERT
     3    FILE PAPERCHEM2
     8    FILE PATDPA
   293    FILE PATDPAFULL
     1    FILE PATOSDE
    29    FILE PATOSEP
    20    FILE PATOSWO
  8917    FILE PCTFULL
     2    FILE PIRA
     8    FILE RAPRA
L1          QUE CHINESE HAMSTER OVARY
            ---------

     FILE 'BIOSIS, TOXCENTER, CAPLUS, MEDLINE, EMBASE' ENTERED AT 09:13:08 ON
     02 JUL 2004
            SET PLURALS ON PERM
            SET ABBR ON PERM
L2       70153 S CHINESE HAMSTER OVARY
L3         285 S CYTIDINE ANALOGUE
L4        9702 S 5-AZACYTIDINE
L5         435 S 5-AZADEOXYCYTIDINE
L6         129 S L2 AND (L3 OR L4 OR L5)
L7          39 DUPLICATE REMOVE L6 BIOSIS  (90 DUPLICATES REMOVED)

=> d L7 1-39 IBIB TI ABS

L7   ANSWER 1 OF 39  BIOSIS  COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER:    2003:173103  BIOSIS
DOCUMENT NUMBER:     PREV200300173103
TITLE:               Chromosomal aberrations induced by 5-
                     azacytidine combined with VP-16 (Etoposide) in
                     CHO-K1 and XRS-5.
AUTHOR(S):           Guimaraes, A. P. A.; Dias, F. L.; Cardoso, R. S.; Kronka,
                     S. N.; Sakamoto-Hojo, E. T. [Reprint Author]
CORPORATE SOURCE:    Departamento de Biologia, Faculdade de Filosofia Ciencias e
                     Letras de Ribeirao Preto, Universidade de Sao Paulo, Av.
                     Bandeirantes 3900, 14040-901, Ribeirao Preto, SP, Brazil
                     etshojo@usp.br
SOURCE:              Teratogenesis Carcinogenesis and Mutagenesis, (2003) No.
                     Supplement 1, pp. 171-186. print.
                     CODEN: TCMUD8. ISSN: 0270-3211.
DOCUMENT TYPE:       Article
LANGUAGE:            English
ENTRY DATE:          Entered STN: 2 Apr 2003
                     Last Updated on STN: 2 Apr 2003
```

TI Chromosomal aberrations induced by **5-azacytidine** combined with VP-16 (Etoposide) in CHO-K1 and XRS-5.

AB A cytogenetic study was carried out with **5-azacytidine** (5-azaC) and etoposide (VP-16) in CHO-K1 and XRS-5 (mutant cells deficient for double-strand break rejoining) cell lines to verify the interaction effects of the drugs in terms of induction of chromosomal aberrations. 5-azaC is incorporated into DNA causing DNA hypomethylation, and VP-16 (inhibitor of topoisomerase II enzyme) is a potent clastogenic agent. Cells in exponential growth were treated with 5-azaC for 1 h, following incubation for 7 h, and posttreatment with VP16 for the last 3 h. In K1 cells, the combined treatments induced a significant reduction in the aberrations induced in the X and "A" (autosome) chromosomes, which are the main target for 5-azaC. However, in XRS-5 cells, the drug combination caused a significant increase in the aberrations induced in those chromosomes, but with a concomitant reduction in the randomly induced-aberrations. In addition, each cell line presented characteristic cell cycle kinetics; while the combined treatment induced an S-arrest in K1 cells, alterations in cell cycle progression were not found for XRS-5, although each drug alone caused a G2-arrest. The different cell responses presented by the cell lines may be explained on the basis of the evidence that alterations in chromatin structure caused by 5-aza-C probably occur to a different extent in K1 and XRS-5 cells, since the mutant cells present a typical hyper-condensed chromosome structure (especially the X- and "A" chromosomes), but, alternatively, 5-aza-C could induce reactivation of DNA repair genes in XRS-5 cells.

L7 ANSWER 2 OF 39 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 2002:458889 BIOSIS
DOCUMENT NUMBER: PREV200200458889
TITLE: DNA methylation and epigenetic inheritance.
AUTHOR(S): Holliday, Robin [Reprint author]; Ho, Thu
CORPORATE SOURCE: Sydney Laboratory, CSIRO Molecular Science, P.O. Box 184, North Ryde, NSW, 2113, Australia
thu.ho@molsci.csiro.au
SOURCE: Methods (Orlando), (June, 2002) Vol. 27, No. 2, pp. 179-183. print.
CODEN: MTHDE9. ISSN: 1046-2023.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 28 Aug 2002
Last Updated on STN: 28 Aug 2002

TI DNA methylation and epigenetic inheritance.

AB Mammalian cell lines silence genes at low frequency by the methylation of promoter sequences. These silent genes can be reactivated at high frequency by the demethylating agent **5-azacytidine** (5-aza-CR). The inactive and active epigenetic states of such genes are stably inherited. A method for silencing genes is now available. It involves treatment of permeabilized cells with 5-methyl deoxycytidine triphosphate (5-methyl dCTP) which is incorporated into DNA. The methylation of promoter sequences has been confirmed using the bisulfite genomic sequencing procedure. Methylated oligonucleotides homologous to promoter sequences might be used to specifically target and silence given genes, but results so far have not been conclusive. Treatments that silence or reactivate genes by changing DNA methylation can be referred to as epimutagens, as distinct from mutagens that act by changing DNA sequences. The epimutagen 5-aza-CR reactivates genes but has little mutagenic activity, whereas standard mutagens (such as ethyl methane sulfonate and ultraviolet light) have little reactivation activity. Nevertheless, much more information is required about the effects of DNA-damaging agents in changing DNA methylation and gene activity and also about the role of epimutations in tumor progression.

L7 ANSWER 3 OF 39 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 1
ACCESSION NUMBER: 1999:342811 BIOSIS
DOCUMENT NUMBER: PREV199900342811
TITLE: Increased levels of DNA topoisomerases in cultured CHO cells treated with the antitumour drug **5-azacytidine.**
AUTHOR(S): Pinero, J.; Lopez-Baena, M.; Ortiz, T.; Mateos, S.; Cortes, F. [Reprint author]
CORPORATE SOURCE: Department of Cell Biology, Faculty of Biology, University of Seville, Avenida Reina Mercedes s/n, E-41012, Seville, Spain
SOURCE: Cytobios, (1999) Vol. 97, No. 385, pp. 103-115. print.
CODEN: CYTBAI. ISSN: 0011-4529.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 24 Aug 1999
Last Updated on STN: 24 Aug 1999

TI Increased levels of DNA topoisomerases in cultured CHO cells treated with the antitumour drug **5-azacytidine.**

AB Cultured **Chinese hamster ovary** (CHO) cells were treated with the **cytidine analogue 5-azacytidine** (5-azaC) which, in good agreement with results previously described from studies carried out in other primary or established mammalian cell lines, resulted in extensive chromosome decondensation and a shift in the time of replication of normally late-replicating heterochromatin to earlier replication. DNA topoisomerases (mainly topo I) have been involved in transcription, and the hypomethylating effect of 5-azaC reportedly results in the expression of silenced genes. Whether such an increase in transcription is paralleled by increased levels of both topo I and topo II, as well as by an enhancement in the topoisomerase activities, has been investigated in this work. The results seem to suggest that both the relative amount of topoisomerases and their activities are enhanced after a protracted treatment with the **cytidine analogue** over those observed in untreated controls. These observations could be significant for antitumour therapy.

L7 ANSWER 4 OF 39 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 2
ACCESSION NUMBER: 2000:121374 BIOSIS
DOCUMENT NUMBER: PREV200000121374
TITLE: Interaction effects of **5-azacytidine** with topoisomerase II inhibitors on CHO cells, as detected by cytogenetic analysis.
AUTHOR(S): Takahashi-Hyodo, Sandra A.; Sakamoto-Hojo, Elza T. [Reprint author]; Takahashi, Catarina S.
CORPORATE SOURCE: Departamento de Genetica e Matematica Aplicada a Biologia, Faculdade de Medicina de Ribeirao Preto, Universidad de Sao Paulo, Sao Paulo, Brazil
SOURCE: Mutation Research, (Dec. 16, 1999) Vol. 431, No. 1, pp. 13-23. print.
CODEN: MUREAV. ISSN: 0027-5107.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 29 Mar 2000
Last Updated on STN: 3 Jan 2002

TI Interaction effects of **5-azacytidine** with topoisomerase II inhibitors on CHO cells, as detected by cytogenetic analysis.

AB Different cell treatment protocols with the hypomethylating agent **5 azacytidine** (5-aza C) were used in exponentially

growing **Chinese hamster ovary** (CHO) cells in order to test its influence on the induction of chromosomal aberrations (CAs) induced by topoisomerase II inhibitors, ellipticine (EPC) and teniposide (VM-26). Cells pre-treated with 1 mug/ml 5-aza C for 1 h during the S-phase and post-treated in the last 2 h of incubation with 0.6 mug/ml EPC or 0.04 mug/ml VM-26 showed a reduction of 48% and 45%, respectively, in the frequencies of CAs as compared to the sum value of the frequencies obtained for each drug alone. 5-aza C added to the cultures for the last 2 h before cell fixation after a 30-min pulse treatment with EPC or VM-26 caused a 38% and 28% reduction, respectively. Simultaneous treatments with 5-aza C plus EPC, or 5-aza C plus VM-26 during the last 2 h of incubation (G2-phase), showed a significant effect of CA reduction (24%) only for the combination of 5-aza C + EPC. Preliminary assays with 5-aza C alone added to the cultures at different times demonstrated its effectiveness in inducing chromosome damage during the S-phase. Since S-phase-treated CHO cells showed a higher degree of reduction in the frequencies of CAs induced by EPC and VM-26, we suggest that 5-aza C incorporation into DNA may change the topo II cleavage sites, protecting the DNA from the induction of damage, or that the hypomethylation induced by incorporation of 5-aza C into DNA may change the chromatin structure facilitating the access to DNA repair enzymes. An alternative possibility is that 5-azaC can reactivate methylated genes involved in the repair of DNA double-strand breaks induced by topo II inhibitors.

L7 ANSWER 5 OF 39 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 3

ACCESSION NUMBER: 1998:485662 BIOSIS
DOCUMENT NUMBER: PREV199800485662
TITLE: Enhanced sensitivity to topoisomerase inhibitors in synchronous CHO cells pre-treated with **5-azacytidine**.
AUTHOR(S): Lopez-Baena, Manuela; Mateos, Santiago; Pinero, Joaquin; Ortiz, Trinidad; Cortes, Felipe
CORPORATE SOURCE: Dep. Biol. Cel., Fac. Biol., Avenida Reina Mercedes, s/n, E-41012 Seville, Spain
SOURCE: Mutation Research, (Oct. 12, 1998) Vol. 421, No. 1, pp. 109-116. print.
CODEN: MUREAV. ISSN: 0027-5107.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 5 Nov 1998
Last Updated on STN: 5 Nov 1998

TI Enhanced sensitivity to topoisomerase inhibitors in synchronous CHO cells pre-treated with **5-azacytidine**.

AB Multidrug combination has been shown to be very useful to improve antitumor activity as well as to reduce the toxicity of different anti-cancer drugs. We have evaluated the interaction between the hypomethylating agent **5-azacytidine** and the topoisomerase I and topoisomerase II inhibitors Camptothecin (CPT) and 4'-(9-acridinylamino) methanesulfon-m-anisidide (m-AMSA) respectively, based on the hypothesis that through the alteration of chromosome replication timing following DNA hypomethylation, the number of replication forks in early S phase might increase, so enhancing the probability of a collision between a blocked cleavable complex (DNA-topo I-CPT or DNA-topo II-m-AMSA) and a replication fork. We have tested the capacity of CPT and m-AMSA to induce chromosomal aberrations as well as reproductive cell death in synchronous cultured **Chinese hamster ovary** cells after a pretreatment with **5-azacytidine** with positive results.

L7 ANSWER 6 OF 39 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

DUPLICATE 4
ACCESSION NUMBER: 1996:447213 BIOSIS
DOCUMENT NUMBER: PREV199699169569
TITLE: Interaction effects between **5-azacytidine** and inhibitors of topoisomerase II in CHO cells, as detected by cytogenetic analysis.
AUTHOR(S): Sakamoto-Hojo, E. T.; Takahashi, S. A.; Takahashi, C. S.
CORPORATE SOURCE: Fac. Filosofia Ciencias Letras, Univ. Sao Paulo, SP, Brazil
SOURCE: Mutation Research, (1996) Vol. 360, No. 3, pp. 267-268.
Meeting Info.: 25th Annual Meeting of the European Environmental Mutagen Society. Noordwijkerhout, Netherlands. June 18-23, 1995.
CODEN: MUREAV. ISSN: 0027-5107.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Oct 1996
Last Updated on STN: 7 Oct 1996
TI Interaction effects between **5-azacytidine** and inhibitors of topoisomerase II in CHO cells, as detected by cytogenetic analysis.

L7 ANSWER 7 OF 39 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 5
ACCESSION NUMBER: 1995:175781 BIOSIS
DOCUMENT NUMBER: PREV199598190081
TITLE: Synergistic and additive combinations of several antitumor drugs and other agents with the potent alkylating agent adozelesin.
AUTHOR(S): Smith, Kathy S.; Folz, Brian A.; Adams, Earl G.; Bhuyan, Bijoy K. [Reprint author]
CORPORATE SOURCE: Cancer Infectious Diseases Res., Upjohn Co., 301 Henrietta St., Kalamazoo, MI 49001, USA
SOURCE: Cancer Chemotherapy and Pharmacology, (1995) Vol. 35, No. 6, pp. 471-482.
CODEN: CCPHDZ. ISSN: 0344-5704.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 26 Apr 1995
Last Updated on STN: 27 Apr 1995
TI Synergistic and additive combinations of several antitumor drugs and other agents with the potent alkylating agent adozelesin.
AB Adozelesin is a highly potent alkylating agent that undergoes binding in the minor groove of double-stranded DNA (ds-DNA) at A-T-rich sequences followed by covalent bonding with N-3 of adenine in preferred sequences. On the basis of its high-potency, broad-spectrum in vivo antitumor activity and its unique mechanism of action, adozelesin has entered clinical trial. We report herein the cytotoxicity for **Chinese hamster ovary** (CHO) cells of several agents, including antitumor drugs, combined with adozelesin. The additive, synergistic, or antagonistic nature of the combined drug effect was determined for most combinations using the median-effect principle. The results show that in experiments using DNA- and RNA-synthesis inhibitors, prior treatment with the DNA inhibitor aphidicolin did not affect the lethality of adozelesin, Therefore, ongoing DNA synthesis is not needed for adozelesin cytotoxicity. Combination with the RNA inhibitor cordycepin also did not affect adozelesin cytotoxicity. In experiments with alkylating agents, combinations of adozelesin with melphalan or cisplatin were usually additive or slightly synergistic. Adozelesin-tetraplatin combinations were synergistic at several different ratios of the two drugs, and depending on the schedule of exposure to drug. In experiments using methylxanthines, adozelesin combined synergistically with noncytotoxic

doses of caffeine or pentoxifylline and resulted in several logs of increase in adozelesin cytotoxicity. In experiments with hypomethylating agents, adozelesin combined synergistically with **5-azacytidine** (5-aza-CR) and 5-aza-2'-deoxycytidine (5-aza-2'-CdR). Combinations of adozelesin with tetraplatin or 5-aza-2'-CdR were also tested against B16 melanoma cells in vitro and were found to be additive and synergistic, respectively. The synergistic cytotoxicity to CHO cells of adozelesin combinations with tetraplatin, 5-aza-CR, or pentoxifylline was not due to increased adozelesin uptake or increased alkylation of DNA by adozelesin.

L7 ANSWER 8 OF 39 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 6

ACCESSION NUMBER: 1996:110149 BIOSIS
DOCUMENT NUMBER: PREV199698682284
TITLE: Persistence of increased levels of ribosomal gene activity in CHO-K1 cells treated in vitro with demethylating agents.
AUTHOR(S): Giancotti, Paola; Grappelli, Claudio; Poggesi, Italo; Abatecola, Marco; De Capoa, Adriana; Cozzi, Renata; Perticone, Paolo [Reprint author]
CORPORATE SOURCE: Cent. Genetica Evoluzionistica CNR, c/o Dipartimento Genetica Biol. Mol., Univ. 'La Sapienza', P. Aldo Moro 5, 00185 Rome, Italy
SOURCE: Mutation Research, (1995) Vol. 348, No. 4, pp. 187-192. CODEN: MUREAV. ISSN: 0027-5107.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 12 Mar 1996
Last Updated on STN: 13 Mar 1996

TI Persistence of increased levels of ribosomal gene activity in CHO-K1 cells treated in vitro with demethylating agents.

AB The rate of ribosomal gene activity was evaluated by silver staining of the Nucleolus Organisers (NOs) in cultured CHO-K1 cells after a 12 h pulse with two demethylating agents (L-ethionine and **5-azacytidine**). Silver staining of the NOs was measured every 24 h, from 24 up to 110 h after seeding. The purpose was to test the hypothesis that drug-induced demethylation is associated to heritable modifications of rDNA activity. Ribosomal gene activity was shown to be significantly increased by both agents. The increase persisted throughout the experiments, thereby suggesting the heritability of this epigenetic modification. The analysis of heritable DNA damage or modification is an important task in studying the risk of cancer onset and the mechanisms of cancer induction. In these studies two main results were obtained: (i) heritable DNA variations can be induced by both mutational and epigenetic changes; (ii) the modified end-point was not negatively selected.

L7 ANSWER 9 OF 39 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 7

ACCESSION NUMBER: 1995:298015 BIOSIS
DOCUMENT NUMBER: PREV199598312315
TITLE: Altered metaphase chromosome structure in xrs-5 cells is not related to its radiation sensitivity or defective DNA break rejoining.
AUTHOR(S): Schwartz, Jeffrey L. [Reprint author]; Brinkman, William J.; Kasten, Lisa; Miller, Daniel W.; Moan, Erich I.; Murphy, Yvonne T.; Stella, Dominick; Sedita, B. A.
CORPORATE SOURCE: Cent. Mechanistic Biol. Biotechnol., Argonne Natl. Lab., 9700 South Cass Ave., Argonne, IL 60439-4833, USA
SOURCE: Mutation Research, (1995) Vol. 328, No. 2, pp. 119-126. CODEN: MUREAV. ISSN: 0027-5107.
DOCUMENT TYPE: Article
LANGUAGE: English

ENTRY DATE: Entered STN: 11 Jul 1995
Last Updated on STN: 11 Jul 1995

TI Altered metaphase chromosome structure in xrs-5 cells is not related to its radiation sensitivity or defective DNA break rejoining.

AB The **Chinese hamster ovary** (CHO) cell line xrs-5 is a radiation-sensitive derivative of CHO-K1 cells. The xrs-5 cells have a defect in DNA double-strand break rejoining and show alterations in chromosome structure and nuclear morphology. The relationship between radiation sensitivity and metaphase chromosome morphology was examined in 12 'revertant' xrs-5 clones isolated following treatment with **5-azacytidine**. Nine of the clones were radioresistant while the other three retained xrs-5-like radiation sensitivity. Chromosome morphology reverted to CHO-K1-like characteristics in three of the radioresistant clones and one of the radiosensitive clones suggesting that the over-condensed metaphase chromosome morphology of xrs-5 cells does not underlie its radiation sensitivity. Radiation sensitivity did correlate with DNA double-strand break rejoining ability. The radioresistant clones showing the over-condensed xrs-5-like chromosome morphology were also slightly more sensitive to the topoisomerase II inhibitor etoposide (VP-16) than CHO-K1, suggesting that the over-condensed morphology might be due to alterations in the phosphorylation of chromatin proteins.

L7 ANSWER 10 OF 39 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 8

ACCESSION NUMBER: 1994:270436 BIOSIS
DOCUMENT NUMBER: PREV199497283436
TITLE: Genetic evidence supporting the role of peroxisome assembly factor (PAF)-1 in peroxisome biogenesis: Polymerase chain reaction detection of a missense mutation in PAF-1 of **Chinese hamster ovary** cells.
AUTHOR(S): Allan, Lee-Ann H.; Hope, Linda; Raetz, Christian R. H.; Thieringer, Rolf [Reprint author]
CORPORATE SOURCE: Merck Res. Lab., P.O. Box 2000, Rahway, NJ 07065, USA
SOURCE: Journal of Biological Chemistry, (1994) Vol. 269, No. 16, pp. 11734-11742.
CODEN: JBCHA3. ISSN: 0021-9258.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 24 Jun 1994
Last Updated on STN: 18 Nov 1994

TI Genetic evidence supporting the role of peroxisome assembly factor (PAF)-1 in peroxisome biogenesis: Polymerase chain reaction detection of a missense mutation in PAF-1 of **Chinese hamster ovary** cells.

AB The peroxisome/plasmalogen-deficient **Chinese hamster ovary** (CHO) mutant cell line ZR-78.1 contains a missense mutation in its cDNA-encoding peroxisome assembly factor-1 (PAF-1). Using a rapid polymerase chain reaction assay, we now demonstrate that the genome of ZR-78.1 contains only the mutant allele. When mutant ZR-78.1 is fused with wild-type karyoplasts, occasional "negative nuclear hybrids" are observed that lack peroxisomes (Allen, L.-A. H., Morand, O. H., and Raetz, C. R. H. (1989) Proc. Natl. Acad. Sci. U. S. A. 86, 7012-7016). Despite the fact that negative nuclear hybrids are tetraploid, they do not contain the wild-type PAF-1 gene, suggesting that a chromosome fragment bearing the wild-type copy of PAF-1 was lost. Negative nuclear hybrids reconstituted with wild-type cytoplasts do contain a wild-type PAF-1 gene, indicating that the cytoplasts somehow reintroduced the wild-type PAF-1 allele without increasing ploidy. These findings support the role of PAF-1 and exclude the hypothesis of an additional cytoplasmic requirement for reinitiation of peroxisome biogenesis in peroxisome-deficient CHO cells. The plasmalogen deficiency

and some other biochemical properties of ZR-78.1 are partially corrected in **5-azacytidine**-treated subclones. However, such pseudorevertants do not contain peroxisomes, consistent with the fact that there is no wild-type PAF-1 gene to reactivate by demethylation.

L7 ANSWER 11 OF 39 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 9

ACCESSION NUMBER: 1993:304847 BIOSIS
DOCUMENT NUMBER: PREV199396023072
TITLE: Enhancement of expression of an introduced gene by **5-azacytidine** in mammalian cell lines.
AUTHOR(S): Tanigawa, Takahiro; Hikida, Masaki; Takai, Toshiyuki; Yasuda, Tatsuji; Ohmori, Hitoshi [Reprint author]
CORPORATE SOURCE: Dep. Biotechnol., Fac. Eng., Okayama Univ., 3-1-1 Tsushima-Naka, Japan
SOURCE: Journal of Fermentation and Bioengineering, (1993) Vol. 75, No. 4, pp. 254-258.
CODEN: JFBIEX. ISSN: 0922-338X.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 23 Jun 1993
Last Updated on STN: 24 Jun 1993

TI Enhancement of expression of an introduced gene by **5-azacytidine** in mammalian cell lines.

AB We transfected a mouse myeloma cell line, P3/NS1-Ag4-1 (NS-1), and a **Chinese hamster ovary** cell line, CHO-K1 with the beta-galactosidase (beta-Gal) gene of Escherichia coli, and isolated stable transformants designated as NS-1Z/gpt and CHO-Z/neo, respectively. When NS-1Z/gpt cells were incubated with 5-20 mu-M **5-azacytidine** (5-azaC), the specific and total activity of beta-Gal were enhanced 2- to 3-fold and 1.5- to 2-fold, respectively In CHO-Z/neo cells, similar treatment resulted in a 3- to 5-fold increase in the specific beta-Gal activity and about a 2-fold enhancements in total enzyme activity. The growth of both cell lines was inhibited by more than 80% in the presence of 10 mu-M 5-azaC. It was confirmed in immunotitration experiments that the enhancement of beta-Gal activities was due to an increase in the enzyme protein. Northern blot analysis revealed that 5-azaC-treatment resulted in the enhanced expression of beta-Gal mRNA. 5-AzaC also enhanced the production of human interleukin 2 (IL2) from CHO cells that were transfected with the IL2 gene. On the other hand, 5-azaC did not significantly affect the expression of an endogenous gene like lactate dehydrogenase or beta-actin. These results suggest that 5-azaC is a useful agent for up-regulating the expression of introduced genes.

L7 ANSWER 12 OF 39 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 1994:38516 BIOSIS
DOCUMENT NUMBER: PREV199497051516
TITLE: An ionizing radiation-sensitive mutant of CHO cells: Irs-20. I. Isolation and initial characterization.
AUTHOR(S): Stackhouse, M. A.; Bedford, J. S. [Reprint author]
CORPORATE SOURCE: Dep. Radiol. Health Sci., Colo. State Univ., Fort Collins, CO 80523, USA
SOURCE: Radiation Research, (1993) Vol. 136, No. 2, pp. 241-249.
CODEN: RAREAE. ISSN: 0033-7587.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 27 Jan 1994
Last Updated on STN: 27 Jan 1994

TI An ionizing radiation-sensitive mutant of CHO cells: Irs-20. I. Isolation and initial characterization.

AB We have isolated a stable mutant of CHO cells, designated irs-20, that is hypersensitive to ionizing radiation. The selection system was designed

to select for mutants unable to proliferate at the low dose rate of 0.06 Gy per hour, a dose rate that has little influence on the effect of radiation on the cell cycle of wild-type cells during 1- to 2-week exposures. The irs-20 mutant cells irradiated continuously at 0.06 Gy/h showed a cell cycle redistribution, with an increasing G-2 + M-phase fraction, but underwent approximately four doublings before cell population growth was completely inhibited. Dose rates three to four times higher were required to produce similar perturbation in the cell cycle of wild-type cells. Asynchronous log-phase irs-20 cells were approximately twofold more sensitive than the parental CHO cells as measured by comparing the doses required to reduce survival to 10%. The survival response of synchronized irs-20 cells after a single radiation dose of 3.8 Gy at different times during the cell cycle was qualitatively similar to the pattern for wild-type CHO cells for an approximately isosurvival dose of 7.4 Gy. The irs-20 cells were hypersensitive to the "radiomimetic" drug bleomycin but showed the wild-type sensitivity to ethyl methane sulfonate, ultraviolet light (254 nm) and mitomycin C. The irs-20 mutant cell has maintained its phenotype for over 1 year in continuous culture, indicating that the defect is genetically stable. The karyotype of the mutant cells is not different from that of its parent. Further evidence of stability is that clonal lines derived from cells surviving high radiation doses also had the irs-20 phenotype, and treatments with **5-azacytidine** sufficient to cause high reversion (apprx 2 times 10-1) to proline independence resulted in no measurable reversion to wild-type radiosensitivity.

L7 ANSWER 13 OF 39 TOXCENTER COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:431050 TOXCENTER
DOCUMENT NUMBER: EMIC-86583
TITLE: **5-AZACYTIDINE** MUTAGENESIS IN AS52 CELLS.
AUTHOR(S): DASTON D L; KELECS ENYI Z; WHITAKER R A; HINES K C; CASPARY W J; TINDALL K R
CORPORATE SOURCE: NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES, RESEARCH TRIANGLE PARK, NC.
SOURCE: Environmental and Molecular Mutagenesis, (1992) 19 (20) 13.
CODEN: EMMUE. ISSN: 0893-6692.
DOCUMENT TYPE: Abstract
FILE SEGMENT: EMIC
OTHER SOURCE: EMIC MUT-92000424
LANGUAGE: English
ENTRY DATE: Entered STN: 20021200
Last Updated on STN: 20021200

TI **5-AZACYTIDINE** MUTAGENESIS IN AS52 CELLS.

AB THE CYTIDINE ANALOG, **5-AZACYTIDINE** (5AC), WAS ORIGINALLY DEVELOPED AS A CHEMOTHERAPEUTIC AGENT AND HAS BEEN SHOWN TO AFFECT CELL DIFFERENTIATION AND TO ALTER GENE EXPRESSION. PREVIOUSLY WE EVALUATED A SERIES OF CYTIDINE ANALOGS, INCLUDING 5AC, FOR THEIR ABILITY TO INDUCE TRIFLUOROTHYMIDINE RESISTANCE (TFTR) IN L5178Y MOUSE LYMPHOMA CELLS [CARCINOGENESIS 10:2003. '89]. WE HAVE EXTENDED OUR STUDIES OF 5AC TO INCLUDE ANALYSES OF MUTATION AT THE GPT LOCUS IN **CHINESE HAMSTER OVARY** (CHO), AS52, CELLS. 5AC IS A POTENT INDUCER OF MUTATION AT THE CHROMOSOMALLY INTEGRATED GPT LOCUS AS DETERMINED BY THE QUANTITATIVE INDUCTION OF 6TGR COLONIES. FOLLOWING A FIVE HOUR TREATMENT, 5AC WAS AN EFFECTIVE MUTAGEN AT ALL CONCENTRATIONS ASSAYED FROM 0.5-5.0 UG/ML. THE MAXIMUM INDUCED MUTANT FREQUENCY (MF) WAS 1350 X 10(-6) VS A SPONTANEOUS MF OF 25 X 10(-6). 5AC TREATMENT RESULTS IN A TYPICAL PHENOTYPIC-EXPRESSION MUTANT-INDUCTION CURVE FOR AS52 CELLS IN WHICH A STABLE MAXIMUM MUTANT FREQUENCY IS OBSERVED 7-9 DAYS FOLLOWING TREATMENT. 6TGR-AS52 CLONES WERE INDUCED FOR MOLECULAR ANALYSES IN TWO EXPERIMENTS WHERE 50 INDEPENDENT CELL CULTURES WERE TREATED WITH 3.0 UG/ML

5AC. THE INDUCED MF RANGED FROM 415-750 X 10(-6). 6GTR CLONES WERE ISOLATED AND DNA WAS PREPARED FOR POLYMERASE CHAIN REACTION (PCR) AND SEQUENCE ANALYSIS. IN THESE STUDIES, ALL CLONES WERE ORGANIZED TO ALLOW AN ASSESSMENT OF CLONAL INDEPENDENCE. THE FREQUENCY OF DELETIONS OR PUTATIVE POINT MUTATIONS WAS DETERMINED BY PCR ANALYSIS. OF 149 6TGR CLONES ANALYZED, 134(90%) WERE PUTATIVE POINT MUTANTS (WILD-TYPE PCR PRODUCT OBSERVED) AND 15(10%) WERE DELETION MUTANTS (ALTERATION OR LOSS OF THE GPT PCR PRODUCT). ALTHOUGH 5AC IS A POTENT CLASTOGEN, THESE DATA SUGGEST THAT 6TG RESISTANCE IN AS52 CELLS FOLLOWING 5AC TREATMENT DOES NOT ARISE PRIMARILY AS THE RESULT OF DELETION MUTATIONS.

L7 ANSWER 14 OF 39 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 10

ACCESSION NUMBER: 1992:282681 BIOSIS
DOCUMENT NUMBER: PREV199294007331; BA94:7331
TITLE: CYTOTOXICITY OF 5 AZA-2'-DEOXYCYTIDINE IN A MAMMALIAN CELL SYSTEM.
AUTHOR(S): DAVIDSON S [Reprint author]; CROWTHER P; RADLEY J; WOODCOCK D
CORPORATE SOURCE: PETER MACCALLUM CANCER INSTITUTE, 481 LITTLE LONSDALE ST, MELBOURNE, VICTORIA 3000, AUST
SOURCE: European Journal of Cancer, (1992) Vol. 28, No. 2-3, pp. 362-368.
CODEN: EJCAEL. ISSN: 0959-8049.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 10 Jun 1992
Last Updated on STN: 10 Jun 1992

TI CYTOTOXICITY OF 5 AZA-2'-DEOXYCYTIDINE IN A MAMMALIAN CELL SYSTEM.

AB After the addition of 5-aza-2'-deoxycytidine, a potent inhibitor of DNA methylation and S-phase-specific cytotoxic agent, metaphase chromosomes of **Chinese hamster ovary** (CHO) cells exhibited a highly decondensed and extended morphology (numerous "fragile sites") at the first mitotic division. However, when a lethal dose of this drug was added in early G1 phase to cells synchronised by mitotic selection, the majority subsequently divided at the same time as an untreated control cell population with few division abnormalities and with few of the more usual types of chromosome aberrations such as gaps, breaks and exchanges. The drug-treated cells also entered and completed the second S-phase without significant delay and it was only at the second mitosis after addition of **5-azadeoxycytidine** that cells showed delays in entering mitosis and significant increases in abnormal divisions concomitant with a modest increase in chromosome aberrations. If cells in a tumour behave similarly, the tumour mass would be expected to double before any reduction in tumour burden could be expected to occur.

L7 ANSWER 15 OF 39 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 1992:206342 BIOSIS
DOCUMENT NUMBER: PREV199242099417; BR42:99417
TITLE: **5 AZACYTIDINE** MUTAGENESIS IN AS52 CELLS.
AUTHOR(S): DASTON D L [Reprint author]; KELECSENYI Z; WHITAKER R A; HINES K C; CASPARY W J; TINDALL K R
CORPORATE SOURCE: NATL INST ENVIRONMENTAL HEALTH SCI, RESEARCH TRIANGLE PARK, NC, USA
SOURCE: Environmental and Molecular Mutagenesis Supplement, (1992) No. 20, pp. 13.
Meeting Info.: 23RD ANNUAL SCIENTIFIC MEETING OF THE ENVIRONMENTAL MUTAGEN SOCIETY, RENO/SPARKS, NEVADA, USA, MARCH 15-19, 1992. ENVIRON MOL MUTAGEN SUPPL.
ISSN: 0898-3003.

DOCUMENT TYPE: Conference; (Meeting)
FILE SEGMENT: BR
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 16 Apr 1992
Last Updated on STN: 2 May 1992
TI **5 AZACYTIDINE** MUTAGENESIS IN AS52 CELLS.

L7 ANSWER 16 OF 39 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 11
ACCESSION NUMBER: 1992:102285 BIOSIS
DOCUMENT NUMBER: PREV199293058835; BA93:58835
TITLE: ACTIVATION OF TWO NEW ALPHA-1 3-FUCOSYLTRANSFERASE ACTIVITIES IN **CHINESE HAMSTER OVARY** CELLS BY **5 AZACYTIDINE.**
AUTHOR(S): POTVIN B [Reprint author]; STANLEY P
CORPORATE SOURCE: DEP CELL BIOL, ALBERT EINSTEIN COLL MED, NEW YORK, NY 10461, USA
SOURCE: Cell Regulation, (1991) Vol. 2, No. 12, pp. 989-1000.
CODEN: CELREQ. ISSN: 1044-2030.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 12 Feb 1992
Last Updated on STN: 13 Feb 1992
TI ACTIVATION OF TWO NEW ALPHA-1 3-FUCOSYLTRANSFERASE ACTIVITIES IN **CHINESE HAMSTER OVARY** CELLS BY **5 AZACYTIDINE.**
AB Several mammalian α(1,3)fucosyltransferases (α[1,3]Fuc-T) that synthesize carbohydrates containing α(1,3)fucosylated lactosamine units have been identified. Although **Chinese hamster ovary** (CHO) cells do not express α(1,3)Fuc-T activity, the rare mutants LEC11 and LEC12, isolated after mutagenesis or DNA transfection, each express an α(1,3)Fuc-T that may be distinguished by several criteria. Two new CHO mutants possessing α(1,3)Fuc-T activity (LEC29 and LEC30) have now been isolated after treatment of a CHO cell population with **5-azacytidine** (5-AzaC), ethylnitrosourea (ENU), or 5-AzaC followed by N-methyl-N'-nitro-N-nitrosoguanidine (MNNG). Like LEC12, both mutants possess an N-ethylmaleimide-resistant α(1,3)Fuc-T activity that can utilize a variety of acceptors and both express the Lewis X (Lex) determinant {Galβ[1,4](Fucα[1,3])GlcNAcβ1} but not the sialylα(2,3)Lex determinant on cell-surface carbohydrates. However, LEC29 and LEC30 may be distinguished from LEC11 and LEC12, as well as from each other, on the basis of their unique patterns of lectin resistance and their abilities to bind the VIM-2 monoclonal antibody that recognizes carbohydrates terminating in NeuNAcα(2,3)Galβ(1,4)Glc-NAcβ(1,3)Galβ(1,4)(Fucα[1,3])GlcNAcβ and also by the different in vitro substrate specificities and kinetic properties of their respective α(1,3)Fuc-T activities. The combined data provide good evidence that the LEC29 and LEC30 α(1,3)Fuc-Ts are novel transferases encoded by distinct gene products.

L7 ANSWER 17 OF 39 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 12
ACCESSION NUMBER: 1991:161419 BIOSIS
DOCUMENT NUMBER: PREV199191087219; BA91:87219
TITLE: HYPOMETHYLATION AND REACTIVATION OF THE ASPARAGINE SYNTHETASE GENE INDUCED BY L ASPARAGINASE AND ETHYL METHANESULFONATE.
AUTHOR(S): WORTON K S [Reprint author]; KERBEL R S; ANDRULIS I L
CORPORATE SOURCE: MOUNT SINAI HOSP, SAMUEL LUNENFELD RES INST, 600 UNIVERSITY AVE, TORONTO, ONTARIO M5G 1X5, CAN

SOURCE: Cancer Research, (1991) Vol. 51, No. 3, pp. 985-989.
CODEN: CNREA8. ISSN: 0008-5472.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 1 Apr 1991
Last Updated on STN: 22 May 1991

TI HYPOMETHYLATION AND REACTIVATION OF THE ASPARAGINE SYNTHETASE GENE INDUCED BY L ASPARAGINASE AND ETHYL METHANESULFONATE.

AB Successful chemotherapeutic treatment of drug-responsive cancers can be compromised by the acquisition of drug resistance. Standard remission induction therapy for childhood acute lymphoblastic leukemia includes L-asparaginase, since the leukemic cells lack asparagine synthetase (AS) activity and require exogenous asparagine. We have used the **Chinese hamster ovary** cell line N3, which lacks AS activity, as a model to examine a novel mechanism involved in the development of drug resistance in acute lymphoblastic leukemia. Expression of AS in **Chinese hamster ovary** cells is associated with hypomethylation in the 5' region of the gene. Activation of AS in concert with hypomethylation occurs spontaneosly at a frequency of about 10-6; we have found that treatment with the hypomethylating drug **5-azacytidine** induces a reversion frequency of 10-2. To investigate the possibility that chemotherapeutic drugs induce similar changes, the asparagine auxotrophic cell line N3 was treated with the chemotherapuetic agents L-asparaginase, vincristine, and 1-β-D-arabinofuranosylcytosine and with the mutagen ethyl methanesulfonate. Both L-aspraginase and ethylmethanesulfonate increased the frequency of reversion to asparagine prototrophy to about 10-5, whereas vincristine and 1-β-D-arabinofuranosylcytosine had no such effect. Asparagine prototrophy correlated with the demethylation of CpG sites in the 5' region of the AS gene and with the appearance of AS mRNA in revertants. In addition to the specific effect seen with the AS gene, L-asparaginase and ethyl methanesulfonate induced global reductions in methylation of up to 20 and 10%, respectively. The ability of chemotherapeutic drugs to inhibit DNA methylation and thereby activate previously silent genes may enable them to promote the aggressiveness of cancers in vivo, including the expression of drug resistance.

L7 ANSWER 18 OF 39 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 13
ACCESSION NUMBER: 1992:142283 BIOSIS
DOCUMENT NUMBER: PREV199293076508; BA93:76508
TITLE: GENE SILENCING IN MAMMALIAN CELLS BY UPTAKE OF 5 METHYLDEOXYCYTIDINE-5'-TRIPHOSPHATE.
AUTHOR(S): HOLLIDAY R [Reprint author]; HO T
CORPORATE SOURCE: CSIRO, DIV BIOMOL ENG, LAB MOL BIOL, PO BOX 184, NORTH RYDE, NSW 2113, AUST
SOURCE: Somatic Cell and Molecular Genetics, (1991) Vol. 17, No. 6, pp. 537-542.
CODEN: SCMGDN. ISSN: 0740-7750.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 12 Mar 1992
Last Updated on STN: 13 Mar 1992

TI GENE SILENCING IN MAMMALIAN CELLS BY UPTAKE OF 5 METHYLDEOXYCYTIDINE-5'-TRIPHOSPHATE.

AB **Chinese hamster ovary** (CHO) cells were subjected to electroporation in the presence of 5-methyl deoxycytidine-triphosphate. This treatment increases by 10 to 100-fold the frequency of cells lacking thymidine kinase, hypoxanthine-guanine phosphoribosyltransferase, or adenine phosphoribosyltransferase. The

inactivation of the genes coding for these enzymes is thought to occur following the direct incorporation of the methylated nucleotide triphosphate into DNA. The enzyme-deficient clones were stable, but almost all were reactivated at high frequency by the demethylating agent **5-azacytidine**, to produce derivatives with enzyme activity. The results indicate that there is a direct relationship between DNA methylation and gene silencing.

L7 ANSWER 19 OF 39 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1991:319785 BIOSIS
DOCUMENT NUMBER: PREV199192030300; BA92:30300
TITLE: INCREASED EXPRESSION OF CHO CELL ENDOGENOUS RETROVIRUS-LIKE PARTICLES DETECTED BY ELECTRON MICROSCOPY AFTER TREATMENT WITH VIRAL INDUCING AGENTS OR CYTOKINES.
AUTHOR(S): MARCUS-SEKURA C J [Reprint author]; KLUTCH M; LUNDQUIST M; DUNLAP R C
CORPORATE SOURCE: DIVISION VIROLOGY, FDA/CBER BLDG 29-A/HFB-500, 8800 ROCKVILLE PIKE, BETHESDA, MD 20892, USA
SOURCE: In Vitro Toxicology, (1991) Vol. 4, No. 1, pp. 13-26. CODEN: IVTOE4. ISSN: 0888-319X.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 15 Jul 1991
Last Updated on STN: 16 Jul 1991

TI INCREASED EXPRESSION OF CHO CELL ENDOGENOUS RETROVIRUS-LIKE PARTICLES DETECTED BY ELECTRON MICROSCOPY AFTER TREATMENT WITH VIRAL INDUCING AGENTS OR CYTOKINES.

AB CHO-K1 cells treated with either 12-O-tetradecanoylphorbol 12-acetate (TPA), **5-azacytidine**, granulocyte-macrophage colony stimulating factor (GM-CSF, human recombinant), tumor necrosis factor (TNF-alpha, human recombinant, or interferon (IFN-alpha, human recombinant) were examined by transmission electron microscopy and a quantitative assessment of retroviral-like particles was made by counting the particles visible in one thin section through 200 different cells for each sample. Scoring included categorizing as to number of particles per cell, type of particle, and location of particle. Control and treated cells contained predominantly type A particles. All treatments increased the number of cytoplasmic particles. The increases varied from 30 to 100%. There was no significant increase in the number of extracellular or budding particles observed in any of the treated samples compared to untreated cells. In the TPA treated samples, there was an increase in the total number of cells scored as containing one or more particles, suggesting that TPA might trigger de novo synthesis or assembly of particles. In addition, in the presence of TPA there was an increase in the total number of intracytoplasmic particles scored. In the presence of GM-CSF, IFN-alpha the total number of intracytoplasmic particles was also increased, particularly centriole-associated particles. **5-Azacytidine** appeared to have little effect on the CHO cell particles, despite its known effect on induction of particles in cell lines of the related Syrian hamster. The absence of particles which could be classified as intracisternal in any of the samples suggested that unlike the situation in other rodent cell lines including the syrian hamster, the CHO cell endogenous particle cannot be considered an intracisternal A particle (IAP).

L7 ANSWER 20 OF 39 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 14
ACCESSION NUMBER: 1990:331212 BIOSIS
DOCUMENT NUMBER: PREV199090039231; BA90:39231
TITLE: MOLECULAR AND GENETICS CHARACTERIZATION OF AN ORNITHINE DECARBOXYLASE-DEFICIENT CHINESE HAMSTER CELL LINE.

AUTHOR(S): PILZ R B [Reprint author]; STEGLICH C; SCHEFFLER I E
CORPORATE SOURCE: DEP BIOL CENTER MOL GENETICS, UNIV CALIFORNIA SAN DIEGO, LA JOLLA, CALIF 92093, USA
SOURCE: Journal of Biological Chemistry, (1990) Vol. 265, No. 15, pp. 8880-8886.
CODEN: JBCHA3. ISSN: 0021-9258.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 24 Jul 1990
Last Updated on STN: 24 Jul 1990

TI MOLECULAR AND GENETICS CHARACTERIZATION OF AN ORNITHINE DECARBOXYLASE-DEFICIENT CHINESE HAMSTER CELL LINE.

AB The ornithine decarboxylase (ODC)-deficient **Chinese hamster ovary** (CHO) cell line C55.7 has normal amounts of ODC mRNA with very low amounts of immunologically detectable ODC protein, suggesting a structural mutation; however, **5-azacytidine** treatment leads to phenotypical reversion (Steglich, C., and Scheffler, I.E. (1985) Somat. Cell Mol. Genet. 11, 11-23). We have demonstrated by chemical cleavage a single mismatch in DNA heteroduplexes composed of wild-type and mutant cDNA strands. DNA sequencing showed that the mutant phenotype results from an aspartate-glycine substitution at amino acid 381 of the protein. When **5-azacytidine**-revertant cell lines were selected for resistance to α-difluoromethylornithine, the resulting amplified ODC gene was structurally indistinguishable from the wild type gene. These results suggested the existence of a single active ODC locus in CHO cells. Using the methylation-sensitive restriction endonucleases AvaI and HpaII, we found evidence for two differentially methylated alleles in wild type, ODC-deficient and α-difluoromethylornithine-resistant cells. One of the alleles appeared completely inactivated by hypermethylation but could be reactivated by demethylation in spontaneous or **5-azacytidine**-induced revertants.

L7 ANSWER 21 OF 39 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 15

ACCESSION NUMBER: 1991:48515 BIOSIS
DOCUMENT NUMBER: PREV199191026796; BA91:26796
TITLE: EVIDENCE FOR ALLELIC EXCLUSION IN **CHINESE HAMSTER OVARY** CELLS.
AUTHOR(S): HOLLIDAY R [Reprint author]; HO T
CORPORATE SOURCE: CSIRO LAB MOL BIOL, PO BOX 184, NORTH RYDE, NSW 2113, AUSTRALIA
SOURCE: New Biologist, (1990) Vol. 2, No. 8, pp. 719-726.
CODEN: NEBIE2. ISSN: 1043-4674.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 10 Jan 1991
Last Updated on STN: 11 Jan 1991

TI EVIDENCE FOR ALLELIC EXCLUSION IN **CHINESE HAMSTER OVARY** CELLS.

AB Earlier results suggested that the functional hemizygosity of genes in pseudodiploid **Chinese hamster ovary** (CHO) cells is due to the silencing of one allele by DNA methylation. From this one could make a strong prediction that we have now been able to confirm by genetic experiments, using thymidine kinase (TK) alleles. TK- mutants induced by ethylmethane sulphonate (EMS) were all revertible to TK+ at high frequency by the demethylating agent **5-azacytidine** (5-aza-CR). This revertibility was due to reactivation of a silent nonmutant TK allele. Further mutagenesis by EMS yielded TK- derivatives that were no longer revertible by 5-aza-CR; these are assumed to have

mutations in both alleles. TK- cells were also transfected with equine herpes virus TK+ DNA, and the TK+ derivatives were shown to be markedly less stable than cells with the normal TK+ gene. CHO cells lack metallothionein activity (sensitive to cadmium), and also require proline for growth, because genes have become silenced during the establishment of the cell line. In both cases 5-aza-CR reactivates these genes to give the cadmium resistant and proline independent phenotypes. Long-term experiments with reactivants in the absence of selection showed that the genes become silent, presumably as a result of de novo methylation. A strain resistant to cytosine arabinoside (araCR) was also resistant to 5-azadeoxycytidien (5-aza-CdR), but not to 5-aza-CR, which would be expected if the araCR strain lacked deoxycytidine kinase. The silent metallothionein gene was reactivated in the araCR strain by 5-aza-CR, but not by 5-aza-CdR, which confirms that the analogs must be incorporated into DNA to induce reactivation. The term allelic exclusion has previously been applied to lymphoid cells that have only one functional immunoglobulin gene. It is proposed that the silencing of one of two alleles in diploid cells by DNA methylation should also be referred to as allelic exclusion.

L7 ANSWER 22 OF 39 TOXCENTER COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:425796 TOXCENTER
DOCUMENT NUMBER: EMICBACK-76217
TITLE: SENSITIVITY OF **CHINESE HAMSTER OVARY** MUTANTS DEFECTIVE IN DNA DOUBLE STRAND BREAK REPAIR TO TOPOISOMERASE II INHIBITORS
AUTHOR(S): JEGGO P A; CALDECOTT K; PIDSLEY S; BANKS G R
SOURCE: Cancer Research, (1989) (49) 7057-7063.
CODEN: CNREA.
DOCUMENT TYPE: (ORIGINAL DATA)
FILE SEGMENT: EMIC
LANGUAGE: English
ENTRY DATE: Entered STN: 20021200
Last Updated on STN: 20021200
TI SENSITIVITY OF **CHINESE HAMSTER OVARY** MUTANTS DEFECTIVE IN DNA DOUBLE STRAND BREAK REPAIR TO TOPOISOMERASE II INHIBITORS

L7 ANSWER 23 OF 39 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 16
ACCESSION NUMBER: 1989:244408 BIOSIS
DOCUMENT NUMBER: PREV198987125473; BA87:125473
TITLE: DEMETHYLATION ENHANCES REMOVAL OF PYRIMIDINE DIMERS FROM THE OVERALL GENOME AND FROM SPECIFIC DNA SEQUENCES IN **CHINESE HAMSTER OVARY** CELLS.
AUTHOR(S): HO L [Reprint author]; BOHR V A; HANAWALT P C
CORPORATE SOURCE: DEP BIOL SCI, STANFORD UNIV, STANFORD, CALIF 94305-5020, USA
SOURCE: Molecular and Cellular Biology, (1989) Vol. 9, No. 4, pp. 1594-1603.
CODEN: MCEBD4. ISSN: 0270-7306.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 20 May 1989
Last Updated on STN: 20 May 1989
TI DEMETHYLATION ENHANCES REMOVAL OF PYRIMIDINE DIMERS FROM THE OVERALL GENOME AND FROM SPECIFIC DNA SEQUENCES IN **CHINESE HAMSTER OVARY** CELLS.
AB We have examined the effects of changes in cytosine methylation on DNA repair in UV-irradiated **Chinese hamster ovary** (CHO) cells. A hypomethylated derivative of the CHO K1B11 line, B11aza, was established by passaging B11 cells over several months in increasing

concentrations of **5-azacytidine**; greater than 60% demethylation was consistently demonstrated in these conditioned cells. Following a UV dose of 10 J/m2, the amount of repair replication performed within 24 h was approximately twofold higher in B11aza cells than in control B11 cells. Removal of T4 endonuclease V-sensitive sites (ESS) from specific restriction fragments within and around the dihydrofolate reductase (DHFR) gene was then examined in B11aza cells and compared with that in B11 cells. Although demethylation had little or no effect on repair in the 5' half of the DHFR gene, within a nontranscribed sequence immediately downstream from the gene, or within an extragenic region further downstream from the DHFR gene, significant increases in repair were observed at the 3' end of the DHFR gene and within an extragenic region upstream of the DHFR gene. However, the increases in DNA repair were not accompanied by any changes in overall cellular resistance to UV when colony-forming ability was assayed. We suggest that the level of DNA methylation may play an indirect role in the regulation of DNA repair, perhaps through an effect on chromatin structure or transcriptional activity.

L7 ANSWER 24 OF 39 TOXCENTER COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:420615 TOXCENTER
DOCUMENT NUMBER: EMICBACK-70737
TITLE: THE LEVEL OF INDUCED SCES SHOWS AN ANOMALOUS PATTERN OF EXTINCTION IN DEMETHYLATED **CHINESE HAMSTER OVARY** CELLS
AUTHOR(S): COZZI R; PERTICONE P
SOURCE: HEREDITAS, (1988) (108) 126.
CODEN: HEREA.
DOCUMENT TYPE: Abstract
FILE SEGMENT: EMIC
LANGUAGE: English
ENTRY DATE: Entered STN: 20021200
Last Updated on STN: 20021200
TI THE LEVEL OF INDUCED SCES SHOWS AN ANOMALOUS PATTERN OF EXTINCTION IN DEMETHYLATED **CHINESE HAMSTER OVARY** CELLS

L7 ANSWER 25 OF 39 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 17
ACCESSION NUMBER: 1989:72765 BIOSIS
DOCUMENT NUMBER: PREV198987037163; BA87:37163
TITLE: CHARACTERIZATION OF X-RAY-HYPERSENSITIVE MUTANT OF V79 CHINESE HAMSTER CELLS.
AUTHOR(S): ZDZIENICKA M Z [Reprint author]; TRAN Q; VAN DER SCHANS G P; SIMONS J W I M
CORPORATE SOURCE: DEP RADIATION GENET CHEM MUTAGENESIS, SYLVIUS LAB, UNIV LEIDEN, WASSENAARSEWEG 72, 2333 AL LEIDEN, THE NETH
SOURCE: Mutation Research, (1988) Vol. 194, No. 3, pp. 239-250.
CODEN: MUREAV. ISSN: 0027-5107.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 23 Jan 1989
Last Updated on STN: 23 Jan 1989
TI CHARACTERIZATION OF X-RAY-HYPERSENSITIVE MUTANT OF V79 CHINESE HAMSTER CELLS.
AB A V79 Chinese hamster cell line XR-V15B exhibiting hypersensitivity to X-ray has been isolated and characterized. Additionally to increased X-ray-sensitivity (approximately 8-fold, as judged by D10 values), cross-sensitivity to bleomycin (3-fold increase), 4NQO (3-fold), H2O2 EMS, MMS (2-fold) were observed also. No increased sensitivity to UV and MMC was found. Genetic complementation analysis indicates that XR-V15B belongs to the same complementation group as the X-ray-sensitive (xrs)

mutants of **Chinese hamster ovary** (CHO) cells described by Jeggo (1985). Biochemical analysis of XR-V15B confirms this finding: the mutant showed a decreased ability to rejoin double-strand breaks induced by X-ray as measured by neutral elution. After 4 h of repair more than 50% of the double-strand breaks remain in comparison to 3% in V79 cells. No difference was observed between wild-type and XR-V15B cells in the initial number of single-strand breaks induced, in the kinetics of their rejoining and in the final level of unrejoined single-strand breaks. Treatment with **5-azacytidine** did not have an effect on the reversion frequency of XR-V15B, contrary to the results obtained with the xrs mutants. XR-V15B has been grown in continuous culture for more than 3 months without evidence of reversion. The mutation induction by X-ray irradiation at the HPRT locus is not significantly increased in the mutant, but at doses giving the same degree of cell killing XR-V15B cells are hypomutable.

L7 ANSWER 26 OF 39 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 18
ACCESSION NUMBER: 1987:443750 BIOSIS
DOCUMENT NUMBER: PREV198784099588; BA84:99588
TITLE: SISTER CHROMATID EXCHANGES INDUCED BY DNA DEMETHYLATING AGENTS PERSIST THROUGH SEVERAL CELL CYCLES IN MAMMALIAN CELLS.
AUTHOR(S): PERTICONE P [Reprint author]; COZZI R; GUSTAVINO B
CORPORATE SOURCE: CENT GENETICA EVOLUZIONISTICA CNR, C/O DEP GNETICA BIOLOGIA MOLECOLARE, UNIV "LA SAPIENZA" PIAZZALE A MORO, 5-00185 ROMA
SOURCE: Carcinogenesis (Oxford), (1987) Vol. 8, No. 8, pp. 1059-1064.
CODEN: CRNGDP. ISSN: 0143-3334.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 24 Oct 1987
Last Updated on STN: 24 Oct 1987

TI SISTER CHROMATID EXCHANGES INDUCED BY DNA DEMETHYLATING AGENTS PERSIST THROUGH SEVERAL CELL CYCLES IN MAMMALIAN CELLS.

AB Eukaryotic DNA methylation has been extensively studied in recent years. The ability of many carcinogens to interfere with DNA methylation has not yet been directly related to their tumorigenic activity. Recent data obtained using L-ethionine and **5-azacytidine**.sbd.both demethylating agents.sbd.showed a small but significant increase in the sister chromatid exchange (SCE) rate induced in mammalian cells (human lymphocytes and CHO cells). In this paper we show that the SCE increase induced by both these agents in **Chinese hamster ovary** (CHO) cells persists for as long as 10 cell cycles. On the other hand mitomycin-C and u.v. light-induced SCEs show a rapid decrease to the control value, as reported for all known SCE inducers. We suggest that DNA demethylation and SCEs are connected through a perturbation of the cell machinery at the level of the replication fork, producing an increase of the error-prone ligation. Since the methylation level is maintained (inherited), the SCE increase produced by these recombinational events will not be corrected through several cell cycles.

L7 ANSWER 27 OF 39 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 19
ACCESSION NUMBER: 1986:397022 BIOSIS
DOCUMENT NUMBER: PREV198682082502; BA82:82502
TITLE: AZACYTIDINE-INDUCED REACTIVATION OF A DNA REPAIR GENE IN **CHINESE HAMSTER OVARY** CELLS.
AUTHOR(S): JEGGO P A [Reprint author]; HOLLIDAY R
CORPORATE SOURCE: GENET DIV, NATL INST MED RES, MILL HILL, LONDON NW7 1AA, UK

SOURCE: Molecular and Cellular Biology, (1986) Vol. 6, No. 8, pp. 2944-2949.
CODEN: MCEBD4. ISSN: 0270-7306.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 4 Oct 1986
Last Updated on STN: 4 Oct 1986

TI AZACYTIDINE-INDUCED REACTIVATION OF A DNA REPAIR GENE IN **CHINESE HAMSTER OVARY** CELLS.

AB Six X-ray-sensitive (xrs) strains of the CHO-K1 cell line were shown to revert at a very high frequency after treatment with **5-azacytidine**. This suggested that there was a methylated xrs+ gene in these strains which was structurally intact, but not expressed. The xrs strains did not complement one another, and the locus was autosomally located. In view of the frequency of their isolation and their somewhat different phenotypes, we propose that the xrs strains are mutants derived from an active wild-type gene. However, there is in addition a methylated silent gene present in the genome. Azacytidine treatment reactivated this gene. We present a model for the functional hemizygosity of mammalian cell lines, which is based on the inactivation of genes by de novo hypermethylation. In contrast to results with xrs strains, other repair-defective lines were found not to be reverted by azacytidine.

L7 ANSWER 28 OF 39 TOXCENTER COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:415493 TOXCENTER
DOCUMENT NUMBER: EMICBACK-65960
TITLE: AZACYTIDINE-INDUCED REACTIVATION OF A DNA REPAIR GENE IN **CHINESE HAMSTER OVARY** CELLS
AUTHOR(S): JEGGO P A; HOLLIDAY R
SOURCE: Molecular and Cellular Biology, (1986) (6) 2944-2949.
CODEN: MCEBD.
DOCUMENT TYPE: (ORIGINAL DATA)
FILE SEGMENT: EMIC
LANGUAGE: English
ENTRY DATE: Entered STN: 20021200
Last Updated on STN: 20021200

TI AZACYTIDINE-INDUCED REACTIVATION OF A DNA REPAIR GENE IN **CHINESE HAMSTER OVARY** CELLS

L7 ANSWER 29 OF 39 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1987:3513 BIOSIS
DOCUMENT NUMBER: PREV198783003513; BA83:3513
TITLE: **5 AZACYTIDINE**-INDUCED CONVERSION TO CADMIUM RESISTANCE CORRELATES WITH EARLY S PHASE REPLICATION OF INACTIVE METALLOTHIONEIN GENES IN SYNCHRONIZED CHO CELLS.
AUTHOR(S): STALLINGS R L [Reprint author]; CRAWFORD B D; TOBEY R A; TESMER J; HILDEBRAND C E
CORPORATE SOURCE: DEP GENETICS, UNIV TEX SYSTEM CANCER CENTER, MD ANDERSON HOSP AND TUMOR INST, 6723 BERTNER AVE, HOUSTON, TEX 77030, USA
SOURCE: Somatic Cell and Molecular Genetics, (1986) Vol. 12, No. 5, pp. 423-432.
CODEN: SCMGDN. ISSN: 0740-7750.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 9 Dec 1986
Last Updated on STN: 9 Dec 1986

TI **5 AZACYTIDINE**-INDUCED CONVERSION TO CADMIUM RESISTANCE CORRELATES WITH EARLY S PHASE REPLICATION OF INACTIVE METALLOTHIONEIN

GENES IN SYNCHRONIZED CHO CELLS.

AB Previous studies have shown both hypermethylation and late replication of DNA sequences to be associated with gene inactivity. To determine whether there is a causal relationship between patterns of DNA methylation and replication timing during S phase, we have examined the timing of replication of the inactive, hypermethylated metallothionein (MT) I and II genes in synchronized, cadmium-sensitive (Cds) CHO cells. The time of S-phase replication of the MT genes was ascertained by (1) determining the period of S phase wherein cadmium-resistant (Cdr) cells could be induced with highest frequency by pulse treatment of synchronized Cds cells with the hypomethylating drug **5-azacytidine** (5-aza-CR), and (2) by analyzing Southern blots of density fractionated DNAs isolated from synchronized cells pulse-labeled with BrdU during different intervals after release from hydroxyurea blockade. Southern filter hybridization analyses demonstrated replication of both MTI and II gene sequences within the first half of S phase. Consistent with this result, phenotypic conversion of Cds to Cdr was maximal immediately after hydroxyurea release and decreased abruptly within three hours. The replication of inactive hypermethylated MT genes in early S phase argues that transcriptional inactivity and gene-specific hypermethylation are not sufficient conditions for late DNA replication.

L7 ANSWER 30 OF 39 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 20

ACCESSION NUMBER: 1986:421920 BIOSIS
DOCUMENT NUMBER: PREV198682097454; BA82:97454
TITLE: INDUCTION OF PROLINE PROTOTROPHS IN CHO-K-1 CELLS BY HEAVY IONS.
AUTHOR(S): MEI M-T [Reprint author]; CRAISE L M; YANG T C H
CORPORATE SOURCE: BIOPHYS LAB, DEP AGRIC BIOL, SOUTH CHINA AGRIC UNIV, GUANGZHOU, PR CHINA
SOURCE: International Journal of Radiation Biology and Related Studies in Physics Chemistry and Medicine, (1986) Vol. 50, No. 2, pp. 213-224.
CODEN: IJRBA3. ISSN: 0020-7616.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 25 Oct 1986
Last Updated on STN: 25 Oct 1986

TI INDUCTION OF PROLINE PROTOTROPHS IN CHO-K-1 CELLS BY HEAVY IONS.

AB Using an established mammalian cell line, **Chinese hamster ovary** cells (CHO-K1), we have observed the induction of prototrophs by various heavy ions. This cell line requires proline for normal growth in medium with low serum concentration. X-rays, three types of heavy particles (600 MeV/u iron, 670 MeV/u neon, and 320 MeV/u silicon ions), ethylmethane sulfonate and **5-azacytidine** were used to induce revertants which were proline independent. Log-phase cells treated with **5-azacytidine** showed a very high reversion frequency. The induction frequency per viable cell appears to be dose dependent for these four types of radiation, and the dose-response curves are approximately linear. Our results also indicate that the effectiveness of high-LET particles in inducing proline prototrophs is much greater than that of low-LET radiation. The RBE value for the induction of prototrophs was calculated for neon, silicon, and iron particles and found to be about 1.3, 1.7 and 4.5, respectively. At equal survival level, the reversion frequency for X-rays and EMS was about the same.

L7 ANSWER 31 OF 39 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 21

ACCESSION NUMBER: 1985:388182 BIOSIS

DOCUMENT NUMBER: PREV198580058174; BA80:58174
TITLE: CORRESPONDENCE BETWEEN EFFECTS OF **5 AZACYTIDINE** ON SISTER CHROMATID EXCHANGE FORMATION CELL CYCLING AND DNA METHYLATION IN CHINESE HAMSTER CELLS.
AUTHOR(S): SHIPLEY J [Reprint author]; SAKAI K; TANTRAVAHI U; FENDROCK B; LATT S A
CORPORATE SOURCE: GENETICS DIVISION, CHILDREN'S HOSPITAL BOSTON, 300 LONGWOOD AVENUE, BOSTON, MASS 02115 USA, USA
SOURCE: Mutation Research, (1985) Vol. 150, No. 1-2, pp. 333-346. CODEN: MUREAV. ISSN: 0027-5107.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

TI CORRESPONDENCE BETWEEN EFFECTS OF **5 AZACYTIDINE** ON SISTER CHROMATID EXCHANGE FORMATION CELL CYCLING AND DNA METHYLATION IN CHINESE HAMSTER CELLS.

AB The effects of **5-azacytidine** (5-Aza-C), alone and in combination with mitomycin C, were measured on sister-chromatid exchange (SCE) formation and DNA methylation in different genomic regions of **Chinese hamster ovary** cells and in Chinese hamster cells containing amplified, dihydrofolate reductase sequences and resistant to methotrexate. 5-Aza-C, when present for the penultimate preharvest cell cycle, induced SCE in a manner consistent with a directly measured reduction in deoxycytosine methylation in cellular DNA. At higher 5-Aza-C concentrations, cell cycling was inhibited and both SCE induction and DNA demethylation tended to level off. Under appropriate conditions, 5-Aza-C potentiated the induction of SCE by mitomycin C. 5-Aza-C-induced DNA demethylation could be detected in the vicinity of different DNA sequences with the use of comparative HpaII/MspI digestion, DNA blotting and molecular probes. The efficiency of an individual demethylation event in inducing SCE induction appeared to be very low, compared with alkylating agents such as 8-methoxypsoralen, suggesting that SCE induction by 5-Aza-C might be an indirect effect from long range changes induced in cellular DNA or chromatin conformation.

L7 ANSWER 32 OF 39 TOXCENTER COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:410728 TOXCENTER
DOCUMENT NUMBER: EMICBACK-61539
TITLE: NEW ARA-C RESISTANT MUTANTS OF THE **CHINESE HAMSTER OVARY** CELLS
AUTHOR(S): MISHRA N C; HINNANT K; CASON E
SOURCE: GENET RES, (1985) (45) 265-277. CODEN: GENRA.
DOCUMENT TYPE: (ORIGINAL DATA)
FILE SEGMENT: EMIC
LANGUAGE: English
ENTRY DATE: Entered STN: 20021200
Last Updated on STN: 20021200

TI NEW ARA-C RESISTANT MUTANTS OF THE **CHINESE HAMSTER OVARY** CELLS

L7 ANSWER 33 OF 39 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 22
ACCESSION NUMBER: 1985:333409 BIOSIS
DOCUMENT NUMBER: PREV198580003401; BA80:3401
TITLE: CHINESE HAMSTER CELLS DEFICIENT IN ORNITHINE DECARBOXYLASE ACTIVITY REVERSION BY GENE AMPLIFICATION AND AZACYTIDINE TREATMENT.
AUTHOR(S): STEGLICH C [Reprint author]; GRENS A; SCHEFFLER I E
CORPORATE SOURCE: DEP MICROBIOL, E CAROLINA UNIV SCH MED, GREENVILLE, NC 27834, USA
SOURCE: Somatic Cell and Molecular Genetics, (1985) Vol. 11, No. 1,

pp. 11-24.
CODEN: SCMGDN. ISSN: 0740-7750.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

TI CHINESE HAMSTER CELLS DEFICIENT IN ORNITHINE DECARBOXYLASE ACTIVITY REVERSION BY GENE AMPLIFICATION AND AZACYTIDINE TREATMENT.

AB A group of **Chinese hamster ovary** (CHO) cell mutants deficient in ornithine decarboxylase (ODC) activity are described and compared to the prototype mutant reported previously. Although all mutants belong to the same complementation group, they can be divided into 2 classes: those with some residual enzyme activity and those with no activity. All mutants are putrescine auxotrophs, but they differ in their ability to utilize the enzyme's substrate, ornithine, a property which correlates with the amount of residual enzyme activity. The mutants also differ in their frequency of reversion to prototrophy. The leaky mutants revert at a high rate by overproducing a partially defective enzyme by a gene amplification mechanism similar to that leading to the ornithine analog-resistant mutants which have elevated enzyme levels. Spontaneous reversion in the null mutants is rare. One null mutant, which was induced with ethyl methanesulfonate and which makes ODC mRNA but no active enzyme, is nevertheless revertible with **5-azacytidine**. CHO cells are at least diploid at the ODC locus, but that only 1 allele is active. Possibly ethyl methanesulfonate is not just a classical mutagen but may also induce gene inactivations that are revertible by **5-azacytidine**.

L7 ANSWER 34 OF 39 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 23
ACCESSION NUMBER: 1984:185870 BIOSIS
DOCUMENT NUMBER: PREV198477018854; BA77:18854
TITLE: COMPLEMENTATION OF MUTATIONS IN THE LOW DENSITY LIPO PROTEIN PATHWAY OF RECEPTOR MEDIATED ENDOCYTOSIS BY CO CULTIVATION OF LOW DENSITY LIPO PROTEIN RECEPTOR DEFECTIVE HAMSTER CELL MUTANTS.
AUTHOR(S): KRIEGER M [Reprint author]
CORPORATE SOURCE: DEP BIOL, WHITAKER COLL HEALTH SCI TECHNOL MANAGEMENT, MASSACHUSETTS INST TECHNOL, CAMBRIDGE, MASS 02139, USA
SOURCE: Cell, (1983) Vol. 33, No. 2, pp. 413-422.
CODEN: CELLB5. ISSN: 0092-8674.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

TI COMPLEMENTATION OF MUTATIONS IN THE LOW DENSITY LIPO PROTEIN PATHWAY OF RECEPTOR MEDIATED ENDOCYTOSIS BY CO CULTIVATION OF LOW DENSITY LIPO PROTEIN RECEPTOR DEFECTIVE HAMSTER CELL MUTANTS.

AB **Chinese hamster ovary** (CHO) cell mutants were isolated that do not express low density lipoprotein (LDL) receptors. When one mutant clone was cocultivated with other receptor-defective clones, it was induced to express receptors that could mediate normal endocytosis. These LDL receptor-defective clones defined 2 classes of mutations: cbc (complemented by cocultivation) and icc (inducer cells in cocultivation). The induction and short-term (18 h) stability of LDL receptors in cbc cells did not require protein synthesis by icc cells. Receptor activity could not be induced by DMSO [dimethyl sulfoxide], **5-azacytidine**, phosphatidylcholine liposomes, dibutyryl cAMP, compactin, soybean trypsin inhibitor, low temperature (30° C), or conditioned medium, but could be induced by cocultivation with parental CHO cells and normal and LDL receptor-negative human fibroblasts. Complementation by cocultivation only occurred when the cbc and inducing cells were in close proximity, suggesting that an unstable diffusible factor or intimate cell-to-cell association was required for

complementation.

L7 ANSWER 35 OF 39 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1984:78812 BIOSIS
DOCUMENT NUMBER: PREV198426078812; BR26:78812
TITLE: CHARACTERISTICS OF **CHINESE HAMSTER OVARY** CELL GENE TRANSFERRENTS ACTIVATION OF HERPES THYMIDINE KINASE GENE BY 5 AZA CYTIDINE TREATMENT.
AUTHOR(S): NAIRN R S [Reprint author]; ADAIR G M; STALLINGS R L; HUMPHREY R M
CORPORATE SOURCE: UNIV TEX SYST CANCER CENT, SCI PARK-RES DIV, PO BOX 389, SMITHVILLE, TX 78957, USA
SOURCE: Journal of Cell Biology, (1983) Vol. 97, No. 5 PART 2, pp. 136A.
Meeting Info.: 23RD ANNUAL MEETING OF THE AMERICAN SOCIETY FOR CELL BIOLOGY, SAN ANTONIO, TEX., USA, NOV. 29-DEC. 3, 1983. J CELL BIOL.
CODEN: JCLBA3. ISSN: 0021-9525.
DOCUMENT TYPE: Conference; (Meeting)
FILE SEGMENT: BR
LANGUAGE: ENGLISH
TI CHARACTERISTICS OF **CHINESE HAMSTER OVARY** CELL GENE TRANSFERRENTS ACTIVATION OF HERPES THYMIDINE KINASE GENE BY 5 AZA CYTIDINE TREATMENT.

L7 ANSWER 36 OF 39 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 83211366 EMBASE
DOCUMENT NUMBER: 1983211366
TITLE: Induction of chromosome decondensation, sister-chromatid exchanges and endoreduplications by **5-azacytidine**, an inhibitor of DNA methylation.
AUTHOR: Hori T.A.
CORPORATE SOURCE: Div. Genet., Natl. Inst. Radiol. Sci., Chiba 260, Japan
SOURCE: Mutation Research, (1983) 121/1 (47-52).
CODEN: MUREAV
COUNTRY: Netherlands
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
022 Human Genetics
016 Cancer
052 Toxicology
LANGUAGE: English
TI Induction of chromosome decondensation, sister-chromatid exchanges and endoreduplications by **5-azacytidine**, an inhibitor of DNA methylation.
AB Mammalian DNAs contain 5-methylcytosine (5mC) as a minor base. Methylation of cytosine residues occurs enzymatically shortly after DNA replication. A number of observations have suggested that this DNA methylation may be involved in gene expression. Incorporation of 5-azaC into DNA inhibits methylation and leads to hypomethylation of DNA. Several studies with 5-azaC have offered evidence for a relation between hypomethylation of DNA and modulations in a variety of gene functions. In an attempt to understand the role of DNA methylation in genome stability, we examined the effect of hypomethylation of DNA induced by 5-azaC on chromosome structure. The experiments were performed with two mammalian cell lines, **Chinese hamster ovary** cells (CHO-K1) and kangaroo-rat cells (KRDO) established from Dipodomys ordii, and human peripheral lymphocytes. The data suggest that the incorporation of 5-azaC into DNA is responsible for the induction of both SCEs and endoreduplications. The present results provide evidence that DNA methylation plays roles in the maintenance of higher-ordered structure of

chromosome and in chromosome sorting in mitosis.

L7 ANSWER 37 OF 39 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 24
ACCESSION NUMBER: 1984:9636 BIOSIS
DOCUMENT NUMBER: PREV198426009636; BR26:9636
TITLE: A STABLE PHENOTYPIC SWITCH FROM CADMIUM SENSITIVITY TO CADMIUM RESISTANCE CORRELATES WITH METALLO THIONEIN 1 AND 2 INDUCIBILITY IN 5 AZA CYTIDINE TREATED CHO CELLS.
AUTHOR(S): HILDEBRAND C E [Reprint author]; ENGER M D; CHEN D J-C; CRAWFORD B D; GRIFFITH J K; MUNK C; WALTERS R A
CORPORATE SOURCE: GENET GROUP, LOS ALAMOS NATIONAL LAB, LOS ALAMOS, NM 87545, USA
SOURCE: Journal of Cell Biology, (1982) Vol. 95, No. 2 PART 2, pp. 451A.
Meeting Info.: 22ND ANNUAL MEETING OF THE AMERICAN SOCIETY FOR CELL BIOLOGY, BALTIMORE, MD., USA, NOV. 30-DEC. 4, 1982. J CELL BIOL.
CODEN: JCLBA3. ISSN: 0021-9525.
DOCUMENT TYPE: Conference; (Meeting)
FILE SEGMENT: BR
LANGUAGE: ENGLISH
TI A STABLE PHENOTYPIC SWITCH FROM CADMIUM SENSITIVITY TO CADMIUM RESISTANCE CORRELATES WITH METALLO THIONEIN 1 AND 2 INDUCIBILITY IN 5 AZA CYTIDINE TREATED CHO CELLS.

L7 ANSWER 38 OF 39 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 25
ACCESSION NUMBER: 1981:226196 BIOSIS
DOCUMENT NUMBER: PREV198172011180; BA72:11180
TITLE: EFFECTS OF DI HYDRO-5 AZA CYTIDINE ON CELL SURVIVAL AND CELL CYCLE PROGRESSION OF CULTURED MAMMALIAN CELLS.
AUTHOR(S): TRAGANOS F [Reprint author]; STAIANO-COICO L; DARZYNKIEWICZ Z; MELAMED M R
CORPORATE SOURCE: INVEST CYTOL LAB, MEML SLOAN-KETTERING CANCER CENT, 1275 YORK AVE, NEW YORK, NY 10021, USA
SOURCE: Cancer Research, (1981) Vol. 41, No. 3, pp. 780-789.
CODEN: CNREA8. ISSN: 0008-5472.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
TI EFFECTS OF DI HYDRO-5 AZA CYTIDINE ON CELL SURVIVAL AND CELL CYCLE PROGRESSION OF CULTURED MAMMALIAN CELLS.
AB The effects of [the antineoplastic drug] dihydro-**5-azacytidine** [5-AC(H): NSC 264880] on cell viability, growth and colony formation were investigated in suspension (Friend leukemia and L1210 [mouse leukemia cells]) and adherent [**Chinese hamster ovary** (CHO)] cell systems as well as in mitogen-stimulated normal human peripheral blood lymphocyte cultures. Cell cycle progression and the terminal point of action of the drug were monitored by flow cytometry. Formation of CHO cell colonies was inhibited by 50% following a 13 h exposure of exponentially growing cells to 25 μg 5-AC(H) per ml or 24 h exposure to 11 μg 5-AC(H) per ml. Stationary cultures required a drug concentration > 10 times higher to reduce colony formation by an equivalent degree. CHO cells during S phase were twice as sensitive as mitotic and G1 cells and 3 times as sensitive as G2 cells to the cytotoxic action of the drug. Drug concentrations of 50 and 35 μg/ml inhibited cell growth by 50% in suspension cultures of Friend leukemia and L1210 cells, respectively. Whereas constant exposure of Friend leukemia cells to 5-AC(H) decreased S-phase cells and increased G2-phase cells, the percentage of S-phase cells in L1210 cultures increased with increasing exposure time and increasing drug concentration;

the higher the dose, the earlier the block was in S phase. Lymphocytes exposed to 5-AC(H) prior to or subsequent to mitogen exhibited diminished stimulation at high (500 µg/ml) drug concentrations. Cellular RNA content was decreased by 20-35% in suspension cultures and in mitogen-stimulated lymphocytes exposed to 200-500 µg 5-AC(H) per ml for 48 h. Detailed analysis of cell cycle progression in L1210 cells in the presence of the drug determined that, while G2-phase cells were refractory to the drug, cell progression through S phase was slowed or halted. The drug decreased the probability of cell exit from the indeterminate (G1A) state but had no effect on the deterministic (G1B) portion of G1 phase.

L7 ANSWER 39 OF 39 TOXCENTER COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:530858 TOXCENTER
DOCUMENT NUMBER: CRISP-94-ES65051-06
TITLE: MOLECULAR ANALYSIS OF POINT MUTATIONS IN **CHINESE HAMSTER OVARY** CELLS
AUTHOR(S): TINDALL K R
CORPORATE SOURCE: NIEHS, NIH
SUPPORTING ORGANIZATION (SPONSORING AGENCY): U.S. DEPT. OF HEALTH AND HUMAN SERVICES; PUBLIC HEALTH SERVICE; NATIONAL INST. OF HEALTH, NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES
SOURCE: Crisp Data Base National Institutes Of Health.
DOCUMENT TYPE: (Research)
FILE SEGMENT: CRISP
LANGUAGE: English
ENTRY DATE: Entered STN: 20021200
Last Updated on STN: 20021200

TI MOLECULAR ANALYSIS OF POINT MUTATIONS IN **CHINESE HAMSTER OVARY** CELLS

AB We use the **Chinese hamster ovary** (CHO) cell line (AS52) with a single functional bacterial gpt transgene stably integrated into the genome to study point mutational changes in mammalian cells. Mutants arise at the gpt locus as 6-thioguanine resistant (6TGr) colonies and are characterized as carrying putative point mutations or deletion mutations using the polymerase chain reaction (PCR). Point mutational spectra are then generated using DNA sequence analysis. We have recently implemented methods in the laboratory to simplify the molecular analysis of mutations in mammalian cells. The site of a mutation in a PCR fragment can be quickly identified prior to DNA sequencing using the HOT (hydroxylamine or osmium tetroxide) modification protocol. Such an approach limits the amount of DNA sequencing necessary and allows for the sequence characterization of a substantially greater number of mammalian mutants. We have evaluated the base analog **5-Azacytidine** (5AC), the anticancer drug, U73,975 and the human carcinogen, Treosulphan, as well as the suspect active metabolite of treosulphan, diepoxy butane (DEB), as mutagens in AS52 cells. All are potent mutagens and mutational spectra have been generated. Among the point mutations induced by 5AC, there is a substantial bias (>90%) for CG>GC transversions. These data suggest a direct role for 5AC as a direct acting mutagen, most likely through the generation of a 5AC:C mispairing during replication. The drug U73,975 is a less toxic analog of the widely studied antitumor drug, CC-1065. In vitro studies of both drugs have revealed preferred DNA binding sequence motifs. Of 125 U73,975- induced mutants analyzed, 44 (35%) are putative point mutants and 81 (65%) are deletions as analyzed by PCR. Among the point mutants, a hot spot for mutations is observed at a site in the gpt gene containing 3-overlapping consensus drug binding sequences. Treosulphan and DEB induce both deletion mutations (70%) and point mutations (30%). These data suggest that Treosulphan and DEB can induce mutations in mammalian cells via at least two mechanistic pathways. DNA sequence analysis is underway to compare point mutational spectra resulting from treosulphan or DEB

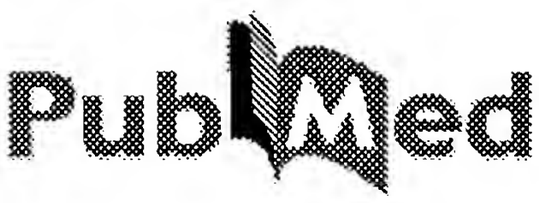
treatment. All of these studies are designed to provide insight regarding the mechanisms by which these agents affect genomic integrity.

=>

---Logging off of STN---

=>
Executing the logoff script...

=> LOG Y



National Library of Medicine

Entrez PubMed Nucleotide Protein Genome Structure OMIM PMC Journals Bl

Search PubMed for Nairn AND chinese hamster ovary AND Thymidine Preview Go Cl

Limits Preview/Index History Clipboard Details

About Entrez

Text Version

Entrez PubMed Overview
Help | FAQ
Tutorial
New/Noteworthy
E-Utilities

PubMed Services
Journals Database
MeSH Database
Single Citation Matcher
Batch Citation Matcher
Clinical Queries
LinkOut
Cubby

Related Resources
Order Documents
NLM Gateway
TOXNET
Consumer Health
Clinical Alerts
ClinicalTrials.gov
PubMed Central

- Search History will be lost after eight hours of inactivity.
- To combine searches use # before search number, e.g., #2 AND #6.
- Search numbers may not be continuous; all searches are represented.
- Click on query # to add to strategy

Search	Most Recent Queries	Time	Result
#1	Search **Nairn AND chinese hamster ovary AND Thymidine kinase**	10:49:50	3
#19	**Related Articles** for **PubMed** (Select **9748718**)	10:47:11	97
#18	**Related Articles** for **PubMed** (Select **8663285**)	10:35:51	356
#10	Search **viral promoter AND chinese hamster ovary**	10:35:43	43
#16	**Related Articles** for **PubMed** (Select **7944334**)	10:27:50	175
#5	Search **Nairn RS**	10:15:12	72

Clear History